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Anemia in Pregnancy: Correlating CD4 Count and Hemoglobin Values among HIV Infected Women

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Authors' contributions

Author LEA conceived and designed the experiments, wrote the protocol, carry out data management and interpretation. Author NAA conceived and designed the experiments, carry out data analysis and interpretation. Author FVS enrolled the patients, performed the experiments, data management. All authors did literature search, prepared the manuscript and read and approved the final manuscript.

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ABSTRACT

Anemia is a common and serious complication in both Human Immunodeficiency Virus (HIV) infection and pregnant women. Anemia has shown to have serious implications for both the mother and her fetus. However, the prevalence of anemia in HIV-infected pregnant women in Cameroon has not been well characterized in the era of highly active antiretroviral treatment (HAART). This study seeks to investigate the correlation between $CD4^+$ count and hemoglobin (Hb) values in pregnant women with HIV infection.

At enrolment, the prevalence of any grade of anemia (Hb < 11 g/dl) was 128(42.2%). The prevalence of anemia was significantly high (p =0.042) in women who were not on treatment 61(49.2%). Moderate grades of anemia 63(20.8%) were common in HIV-infected patients while 3 of the 4 cases of severe grades of anemia were common in patients who were on HAART. The low prevalence of anemia among treated HIV-infected, pregnant women indicate that the treatment of all HIV positive pregnant women at the first antenatal visit is essential.

Keywords: Anemia; HIV; pregnant women; hemoglobin; CD4+ T cells count.

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1. INTRODUCTION

Anemia and HIV are serious public health problems in pregnancy and a major cause of maternal death [1,2]. Anemia is a preventable complication and has been associated with decreased quality of life [1,3]. In pregnancy, anemia is associated with poor birth outcomes such as increased risk of stillbirths, low birth weight, intrauterine growth restriction, neonatal sepsis as well as increase risk of perinatal maternal mortality [3-4]. It is estimated that 24.8%-75% of pregnant women worldwide are anemic [1,2,5,6]. This prevalence is reported to be high (52-75%), in low resource countries compared to 12–25% in developed countries [3,7]. In Cameroon, the prevalence ranges from 50-57% [8].

The number of pregnant women living with the HIV globally continues to increase [2,9]. In Cameroon, the prevalence of HIV-1 ranges from 3.6-4.3% among the general population [10,11] and ranges from 5-17.4% among pregnant women [12-15]. HIV in pregnancy has shown to present with a severe adverse outcome such as spontaneous abortion, premature delivery, intrauterine growth restrictions, low birth weight infants, obstetric hemorrhage, obstetric shock and trauma due to labour complication and possible HIV transmission to both the mother, infant and health workers during delivery [3,13,15].

Anemia is the most common hematological abnormality in HIV patients and HIV-infected pregnant women have shown to present with significantly lower hemoglobin concentrations compared to HIV uninfected pregnant women [5]. Although the burden of anemia in HIV/AIDS patients is not very well understood, several studies in Sub-Saharan Africa have identified anemia prevalence of 30-80% or higher in HIV-infected pregnant women [2,7,16]. The incidence of anemia is strongly associated with the progression of the disease and is the cause of high morbidity and mortality among HIV-infected pregnant women due to its devastating effect on the human $CD4^+$ T cell counts [5,17].

Although anemia associated with HIV leads to increased morbidity and mortality during pregnancy, the prevalence of anemia in HIV-infected persons has not been well characterized in Cameroon which we seek to investigate. Besides, we will evaluate and compare the correlation of $CD4^+$ T cell count and hemoglobin (Hb) values among naïve and treated HIV-positive pregnant women. Thus this study on the correlation of Hb count and $CD4^+$ T cell count are important in the design of public health and clinical interventions targeting the management of anemia in HIV-infected women.

2. METHODOLOGY

2.1 Study Design

This study was a cross-sectional and prospective hospital-based study undertaken at five (5) antenatal clinics of the Northwest region of Cameroon from April 2017 to March 2018. These clinics included both government and faith-based institutions. The study population included HIV seropositive pregnant women attending first ANC. At enrolment, a structured questionnaire was used to document socio-demographic characteristics (age, residence, and marital status), gynaecologic history (gestational age) and socio-economic indicators (educational level and monthly income).

2.2 Study Site and Population

The women were enrolled from Regional hospital Bamenda, Centre médical d'arrondissement (CMA) Nkwen, St. Mary Soledad hospital Mankon, Ndop District Hospital, and Saint John the Baptist Health Center Ndop. All the women gave their consent. A total of 303 women between the ages of 16 and 43years were recruited into the study.

2.2.1 Inclusion and exclusion criteria

HIV positive pregnant women attending first antenatal care, at least 15 years of age and gave her consent were included into the study. While exclusion criteria were pregnant women with other medical conditions (e.g. tuberculosis, endocarditis and acute viral infections) which could affect blood count, refused to sign the inform concern form and was looking severely ill.

2.3 Data Collection

Data collection was obtained from the participants records with complete information on socio-demographic (age, residence, level of education, monthly income and marital status), immunological and obstetric history, (current $CD4^+$ T cell count, parity, gestational age, and treatment history of those who already knew their HIV status).

2.4 Laboratory Procedure

A total of 4.0 ml of venous blood was collected and transferred into a tube containing ethylene diamine tetraacetic acid solution and used to measure $CD4^+$T cell count and Hemoglobin levels.

2.4.1 $CD4^+$T cell count

The enumeration of $CD4^+$ T cell counts was done using PIMA machine as describe by Thakar et al. [18].

2.4.2 Hemoglobin level

Haemoglobin concentrations were determined using a hemosmart gold meter (Haemocue AB, Angelholm, Sweden) using the manufacturer's procedure [19].

2.4.3 Definitions of anemia

Anemia was defined as Hb < 11.0 g/dl. Anemia severity was classified as follows: mild anemia (Hb: 10–10.9 g/dl), moderate anemia (Hb: 7–9.9 g/dl), and severe anemia (Hb < 7.0 g/dl) using WHO standards [8].

2.5 Data Analysis

Data was entered and analyzed using the statistical package for social sciences (SPSS) version 23.0, (Chicago, USA). Descriptive statistics were done and summarized by frequencies and proportions for categorical predictors. The occurrence of anemia was compared among the cohort using chi-square. The independent sample T-test was used to compare means. Correlation between $CD4^+$ T-cell count and hemoglobin levels were evaluated using Spearman ranked correlation coefficient. *P* <0.05 was considered to be statistically significant.

3. RESULTS

3.1 General Characteristics of the Study Population

The demographic and obstetrical characteristics of the participants are summarized in Table 1. The mean ±standard error of mean (SEM) age of the study participants was 28.26± 0.46years and ranged from 16-43 years. The majority of the women 110(36.3%) were in the >35year age-group, and more than half 213(70.3%) were married or cohabiting. The subjects were fairly educated, as close to half 144(47.5%) of the participants had attained secondary school education. More than half 191(63.0%) of the participants were from urban areas and had a monthly income of <50,000Frs (80USD); 235(77.6%). Most of the women 179(59.1%) knew their HIV status and were on treatment. In addition more than half 253(83.5%) of the study population began ANC clinic at second trimester with a mean± SEM gestational age of 19.1 ±0.362 weeks that ranged from 2-37 weeks.

3.2 Anemia Prevalence

At enrolment, mean (SEM) Hb was 11.12 (0.09)g/dL and 128(42.2%) participants had anemia (Hb<11.0 g/dL). Majority of the women 63(20.8%) who were anemic presented with moderate anemia (Hb between 7-9 g/dL) and 61(20.1%) had mild anemia (Hb between 9.1-10.9 g/dL), while the least participants 4(1.3%) were severely anemic (Hb<7 g/dL). The prevalence of anemia was significantly high (p =.042) in women who were not on treatment 61(49.2%) compared to those on treatment 67(37.4%).

Anemia was high among women of the age group >30years; 49(44.5%), women who were single, widow or divorced 48(53.3%), women who attended primary education 68(48.9%), women leaving in urban area 88(46.1%), those with low monthly income 100(42.6%), $CD4^+$ T cell count of <200 cells/mm^3 57(47.1%) and women who began ANC at first trimester 18(54.5%). With the exception of marital status (p=0.011) these differences were not significant (Table 2).

3.3 Hemoglobin Level and $CD4^+$ T Cell Count

The $CD4^+$ T cell count and a hemoglobin level of treated pregnant women were significantly higher (p =.037 and p=.000 respectively) when compared to treatment naïve women (Table 3). In Fig. 1, Spearman's rank correlation showed a positive correlation between $CD4^+$ T cell count and Hb (r =0.087, p =.037).

Table 1. Demographic and obstetrical characteristics of 303 pregnant women by treatment intervention

Variable	Total participants N= 303(%)	On HAART		P-value
		No 124 (40.9%)	Yes 179 (59.1)	
Demographic characteristics				
Age (year) ; 95%CI; 1.35-1.50				
Mean ± SD (range)	28.26±0.36 (16-43)	28.29±0.46 (16-43)	28.22±0.56 (16-42)	.912
<25	94(31.0)	38(40.4)	56(59.6)	.987
25-30	99(32.7)	41(41.4)	58(58.6)	
>30	110(36.3)	45(40.9)	65(59.1)	
Marital Status				
Single, widow, divorced	90(29.7)	37(41.4)	53(58.9)	.966
Married/Cohabiting	213(70.3)	87(40.8)	126(59.2)	
Educational level				
None	3(1.0)	0(0.0)	3(100.0)	.12
Primary	139(45.9)	61(43.9)	78(56.1)	
Secondary	144(47.5)	53(36.8)	91(63.2)	
Tertiary	17(5.6)	10(58.8)	7(41.2)	
Address				
Urban	191(63.0)	78(40.8)	113(59.2)	.965
Rural	112(37.0)	46(41.1)	66(58.9)	
Monthly income(in CFA frs)				
<50000(80USD)	235(77.6)	91(38.7)	144(61.3)	.152
>50000(80USD)	68(22.4)	33(48.5)	35(51.5)	
Immunological characteristic; $CD4^+$; (95% CI; 27.61-88.74) cells/mm^3				
<200	121(39.9)	65(53.7)	56(46.3)	.001
200-350	129(42.6)	44(34.1)	85(65.9)	
>350	53(17.5)	15(28.3)	38(71.7)	
Gestational age classification (95% CI; 0.80-2.09)				
First	33(10.9)	16(48.5)	17(51.5)	0.233
Second	253(83.5)	104(41.1)	149(58.9)	
Third trimester	17(5.6)	4(23.5)	13(76.5)	

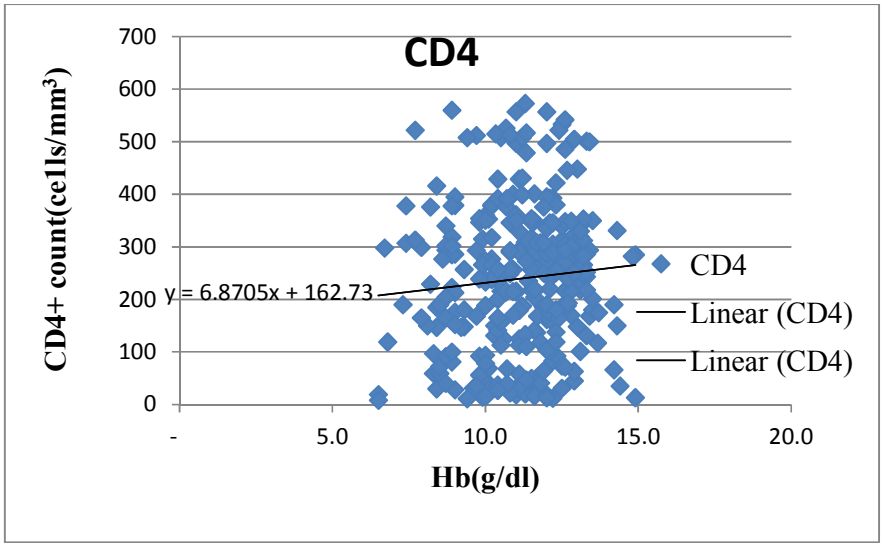

Fig. 1. Scatter diagram showing the distribution of the $CD4^+$ T cell plotted against haemoglobin (Hb) levels

Table 2. Prevalence of anemia by demographic and obstetrical characteristics

Variable	Total participants N= 303(%)	Anemia		x^2 (P-value)
		No 175 (57.8%)	Yes 128 (42.2)	
Age groups in years				
<25	94(31.0)	56(59.6)	38(40.4)	5.25(0.072)
25-30	99(32.7)	58(58.6)	41(41.4)	
>30	110(36.3)	61(55.5)	49(44.5)	
Marital status				
Single, widow, divorced	90(29.7)	42(46.7)	48(53.3)	6.45(0.011)
Married/Cohabiting	213(70.3)	133(62.4)	80(37.6)	
Educational level				
None	3(1.0)	3(100.0)	0(0.0)	6.84(0.077)
Primary	139(45.9)	71(51.1)	68(48.9)	
Secondary	144(47.5)	89(61.8)	55(38.2)	
Tertiary	17(5.6)	12(70.6)	5(29.4)	
Address				
Urban	191(63.0)	103(53.9)	88(46.1)	3.105(0.078)
Rural	112(37.0)	72(63.4)	40(35.7)	
Monthly income in CFA Frs				
<50000(80USD)	235(77.6)	135(57.4)	100(42.6)	0.41(0.84)
>50000(80USD)	68(22.4)	40(41.2)	28(41.2)	
$CD4^+$ T cell count cells/mm^3				
<200	121(39.9)	64(52.9)	57(47.1)	3.158(0.206)
200-350	129(42.6)	82(63.6)	47(36.4)	
>350	53(17.5)	29(54.7)	24(45.3)	
Gestational age classification				
First	33(10.9)	15(45.5)	18(54.5)	3.251(0.197)
Second	253(83.5)	148(58.5)	105(41.5)	
Third trimester	17(5.6)	12(70.6)	5(24.9)	

Table 3. Mean Hb and CD4+ T cell count (cells/µl) of treated and non-treated pregnant women

Variable	On HAART		P-value
	No 124 (40.9%)	Yes 179 (59.1%)	
Haemoglobin (g/dl)	10.88±0.15	11.08±0.12	.052
CD4+ count(cells/mm^3)	204.75±11.43	262.93±10.21	.000

4. DISCUSSION

The results of this study demonstrate that the majority 110(36.3%) of the study participants were in the >35years age-group and most of them (70.3%) were married or cohabiting. This is due to increase sexual encounter that comes with marriage as well as living together with the opposite sex. Besides, it might be due to the high number of people with multiple sexual partners that predispose this population at high risk of acquiring HIV infection. The subjects were fairly educated, indicating an increasing need for sensitization on safe sex and sex education within the community.

The major finding in this study indicates that 42.2% of the participants had anemia at first ANC. Previous studies carried out in South Africa and Kenya have reported a prevalence range of 44-83% in persons living with HIV [20,21]. However, data from this study was slightly below the range for other previous studies. This result is higher when compared to Nandlal et al. [20] which reported that 1.8% of the women were free from anemia at enrolment. This high prevalence could be attributed to the fact that most of our study participants 253(83.5%) were recruited in the second trimester of pregnancy. Secondly our population was from a low socio-economic setting as 235(77.6%) of the women had a monthly income of <50000 CFA frs (80USD) as such malnourishment and various socioeconomic factors may lead to anemia. In addition the high prevalence could be due to iron deficiency since these women had not receive the routine iron

therapy. High anemia level in low economic status women might be due to financial constrains that may hinder access to iron rich diet such as animal proteins and dietary supplementation. Furthermore, the high prevalence of anemia registered in women who began ANC at first trimester can also be attributed to the low economic status of these women that may delay early initiation of ANC and uptake of anemia preventive treatment. In addition the high level of anemia in women attending ANC at first trimester might be due to the fact that these women might be suffering from other health problem such as malaria which can lead to anemia [21,22]. Pregnant women aged >30 years were more anemic compared to those younger. This result is in agreement with the previous study conducted in Kenya [6]. Most probably the high prevalence might be due to multiple pregnancies that has shown to be a risk factor for the development of anemia.

The prevalence of anemia was significantly high (49.2 %) in women who were not on HIV treatment compared to those on treatment (37.4%). This conforms to earlier reports which state that low levels of hemoglobin may be associated with AIDS and death in people with HIV [23]. This finding is similar to that of Nandlal et al. [20] and Odhiamo et al. [21] whose studies showed that women with higher $CD4^+$ T cell counts were less likely to develop anemia. Studies have shown that HIV infection is known to suppress erythropoietin and thus low serum folate, vitamin B12, and ferritin levels in pregnancy [2]. Thus the low prevalence of anemia among women on treatment indicates that the HIV disease is under control compared to those who were not yet on treatment. Furthermore, it has been reported that, risk of malarial fever increase with decreasing $CD4^+$ T cell count and increasing viral load [22] thus high levels of $CD4^+$ T cell count will prevent malaria which is one of the leading cause of anemia.

Data from this study also reported that 75% (3/4) of women with severe anemia were HIV-positive women on treatment even though these women presented with high $CD4^+$ T cell counts. This is probably due to HAART since HAART especially Zidovudine base treatment-induced anemia [1,2].

Furthermore, correlation studies revealed a highly significant positive correlation between hemoglobin and $CD4^+$ T cell counts (Fig. 1). This positive correlation was in accordance with previous studies [22,23-26]. The positive correlation can also be attributed to the use of HAART that leads to increase $CD4^+$ T cell counts and thus will reduce the negative effect of HIV on erythropoiesis. Although the use of $CD4^+$ T cell counts in monitoring disease progression, drug initiation and treatment has been discouraged, the significant positive correlation between hemoglobin levels and $CD4^+$ T cell count indicates that the use of the Hb measurement which is simple and inexpensive could be used in low income or economically disadvantaged settings where it is difficult to monitor $CD4^+$ T cell counts due to power failure, lack of reagents or breakdown of the machine to provide prognostic information by the $CD4^+$Tcell counts.

5. CONCLUSIONS

The major findings in this study are the high prevalence (42.2 %) of anemia recorded in HIV pregnant women. There was a strong positive correlation between Hemoglobin and $CD4^+$ T cell counts. Thus, anemia is a common finding in pregnant women diagnosed with HIV with high perinatal and maternal morbidity rates. Therefore HIV-positive pregnant women require special attention and follow-up to reduce the risk of maternal death and adverse pregnancy outcomes resulting from the effects of anemia.

6. LIMITATION

The type of drug used in the treatment of HIV could not be assessed because the treatment was based on the drugs available at the moment.

CONSENT AND ETHICAL APPROVAL

Ethical approval was obtained from the Delegation of Public health and Ethical Committee of the various institutions before data collection and patient recruitment. Each patient gave her consent after the objectives and procedures to be carried out were explained to them.

COMPETING INTERESTS

Authors have declared that no competing interest exist.

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